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TRANSLATION FROM RUSSIAN*. CHUMAKOV, M. P. (1965)**. A short review of investigation of the virus of Crimean hemorrhagic fever. In: Chumakov, M. P. (ed.). Endemic viral infections (Hemorrhagic fever with renal syndrome, Crimean hemorrhagic fever, Omsk hemorrhagic fever, and Astrakhan virus from Hyalomma pl. plumbeum tick). /Sborn. Trud. Inst. Polio. Virus, Encephal., Akad. Nauk USSR, (Medicine, Moscow), (7), pp. 193-196.

Etiological study of Crimean hemorrhagic fever (CHF) began in 1944, when outbreak of this illness consisting of 200 cases was observed for the first time in Crimea (Collection: "Crimean hemorrhagic fever". Edited by I. E. Sokolov, A. A. Kolchav, M. P. Chumakov). The first ordinary serodiagnostic, bacteriological, leptospiral, and rickettsiological investigations of patients and convalescents as well as some animal species including mice, rats, guinea pigs, rabbits, cats, chick embryos, chicks, rhesus monkeys, hamadryas baboons, lambs, piglets, and hedgehogs gave completely negative or dubious results (M. P. Chumakov, 1947). Data obtained in this manner did not exclude the viral nature of the Crimean hemorrhagic fever agent, but pointed out considerable difficulties in detecting the activity of such virus in ordinary experiments on animals. Already in 1945, an initial study of the Crimean hemorrhagic fever agent proved to be successful in observations on mental patients, who according to medical reports and health conditions required pyrogenic therapy. These observations (Chumakov, M. P., Vereshilova, M. K., Belyaeva, A. P., quoted by Chumakov, M. P., 1946) have determined the essential questions concerning the characteristics of the agent of Crimean hemorrhagic fever. This agent proved to be a filterable virus present in blood sera of patients during the acute stage of illness. The virus was also found in steppe ticks (nymphs and adult) Hyalomma pl. plumbeum (or according to old terminology: Hyalomma marginatum marginatum) ***.

In one positive case, hungry adult (unengorged) Hyalomma pl. plumbeum ticks were collected in Crimea in early spring. This proved the long existence of the virus of Crimean hemorrhagic fever in the vector, and in any case, the possibility of its overwintering in ticks. Viral gical examination of herds' blood during the period of mass infestation by larvae and nymphs of ticks in Crimea, gave negative results. However, in isolation of the virus of Crimean hemorrhagic fever from nymphs of Hyalomma pl. plumbeum collected from the herds was successfully accomplished.

This translation is made for members of the U.S. Hemorrhagic Fever Delegation to the USSR and for other interested persons.

* The Institute of Poliomyelitis and Viral Encephalitis for the Medical Academy of the USSR.

** Terminology of western workers (HH).

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(M. P. Chumakov, 1947-1952). It is possible that Hyalomma pl. plumbeum tick plays the role of a vector and an independant reservoir of the virus as it has been established for Ixodes persulcatus and Ixodes ricinus in relation to human tick-borne encephalitis (Shubladze, A. K. and Sordynkova G. V., 1939; Chumakov, M. P., 1939-1944).

These observations (Chumakov, M. P., Vereshilova, M. K., Belyaeva M. P., 1945-1946), demonstrated that a person who had Crimean hemorrhagic fever develops a very strong immunity against repeated introduction of the virus. Virus strains recovered from CHF patients' blood and from ticks Hyalomma pl. plumbeum proved to be immunologically identical. Antigenic identity of some virus strains was revealed by a neutralisation test by passing strains of the virus through the sera of convalescents who had recovered from the experimental or from natural illness. It is important to note that attempts to produce cross-neutralisation of the viruses of Crimean hemorrhagic fever with sandfly fever (pappataci) gave clearly negative results; negative results were also obtained from the neutralization reaction of the virus by serum of hemorrhagic nephro-nephritis convalescents in the Far East, which proves that these viral diseases are independant.

Application of complement fixation reaction in serodiagnosis of Crimean hemorrhagic fever by Loeffler's and his colleagues' method gave already in 1956 conclusively positive results (Khai, L. M., Belyaeva, M. P.). It was convenient in this reaction to use as antigen blood sera from patient during the first 2 or 3 days after elevation of body temperature, which corresponds to the period of acute viromia.

Revealing the antigen in the blood of febrile patients by complement fixation test in which tested convalescent serum (from 35-40 days to 1-2 years) is used as an antibody, guarantees in early serodiagnosis of Crimean hemorrhagic fever. One must admit that the method of determining the viral antigen by complement fixation test is not suitable for practical diagnosis, because of complexity of the serum reaction with complements, and also because of the impossibility to preserve active serum that is not complemented with immune serum. In order to produce antibodies against the virus of Crimean hemorrhagic fever, another source of antigen for complement fixation reaction must be found.

Attempts to cultivate the agent of Crimean hemorrhagic fever on some primary and transplantable cells in vitro were undertaken repeatedly (in 1946-1955). However, conclusions were negative in view of the absence of any noticeable cytopathogenic changes in chick embryo and human fibroblast cells utilized for inoculation (Chumakov, M. P., 1960, based on M. P. Belyaeva's experiments). Recently however, observations of cultivation of Crimean hemorrhagic fever have broadened considerably in scope (Belyaeva, M. P. with colleagues, 1964, Semashko, I. V. with colleagues, 1965). The same is true of observations of the phenomena of interference (Shalunova, N. V. with coll., 1965) utilized for specific indication of the CHF virus in tissue cultures, adjusting the regular cultural passages of the virus, and studying and isolating in vitro many new strains from 2 endemic regions

This collection contains new data on the potential and already obtained results in applying cultural methods in study of the Crimean hemorrhagic fever agent. The unexpected discovery of the ability of the Crimean hemorrhagic fever to induce cytopathogenic changes in infected cell line cultures, and clear formation of plaques in some cell cultures under the layer of agar came as a surprise (Shalunova, N. V., Smashko, I. V., Chumakov, M. P., 1965). This opens new possibility for serodiagnosis of Crimean hemorrhagic fever by a neutralization reaction in tissue cultures, as well as for other prospects in study of the Crimean hemorrhagic fever virus.

In this short outline, it is important to mention results of virological study of the so called Uzbekistan hemorrhagic fever, obtained between 1949 and 1952 by N. I. Khodukin and his colleagues. Hemorrhagic fever in Uzbekistan as in other Central Asiatic republics and in Kazakhstan, shows undisputedly great resemblance to Crimean hemorrhagic fever, with the only exception, that its probable participant in transmission are other species of ticks, although close to Hyalomma anatolicum ticks. Professor N. I. Khodukin has acknowledged this resemblance or identity with Crimean hemorrhagic fever, although taking into account possible differences in vectors and different peculiarities of foci, considered it necessary for the present to distinguish carefully Central Asiatic incidence of hemorrhagic fever as independent form of infection.

Despite the certainty concerning viral etiology of hemorrhagic fever in Uzbekistan, N. I. Khodukin and his colleagues were not able to obtain convincing evidence to prove their theory; experiments of inoculating rabbits and employing thus obtained antigens and immune sera in Complement fixation test, may produce unspecific (false positive) results. It was impossible to decide with certainty the problem of viral etiology of the Crimean hemorrhagic type of illness without observations carried out on people. However, recently with the invention of a new technique of cultivation and identification of the Crimean hemorrhagic fever virus, it became possible to explain the interrelation between Crimean hemorrhagic fever and other illnesses of this type encountered in Central Asiatic republics, in Kazakhstan, and in other countries.

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